target site and present at the target site and at least one second binding site which specifically binds to an epitope of at least one enzyme, wherein binding between the targeting protein and the enzyme does not interfere with enzyme activity;

(b) optionally, administering to the patient an amount effective for clearance of a first clearing composition comprising a clearing agent which clears non-localized targeting protein from circulation;

B1 Conclude

(c) administering to the patient an effective amount for enzyme activity of the enzyme, such that the targeting protein binds the enzyme to form a non-covalent targeting protein-enzyme conjugate *in situ*;

(d) optionally, administering to the patient an amount effective for clearance of a second clearing composition comprising a clearing agent which clears non-localized targeting protein, non-localized enzyme, or non-localized targeting protein-enzyme conjugate from circulation;

(e) administering to the patient at least one serum-soluble prodrug composition, wherein the enzyme administered in step (c) acts on the prodrug to release a therapeutic agent that is less soluble in serum than the prodrug, and wherein the therapeutic agent partitions out the target site that it accretes at the target site to a greater extent than would the prodrug, thereby providing therapeutic agent at the target site.

B2

33. (Amended) The method of claim 1, wherein the targeting protein, the enzyme, or both, comprises a therapeutic agent such that step (c) results in the *in situ* formation of a targeting protein-enzyme conjugate comprising a therapeutic agent that is different from a therapeutic agent of the prodrug.

B3

40. (Amended) The method of claim 39, wherein at least about 48% of lysine residues of the clearing agent are modified with sugar residues.